

## General

### Guideline Title

Locoregional therapy of locally advanced breast cancer (LABC).

## Bibliographic Source(s)

Brackstone M, Fletcher GG, Dayes IS, Madarnas Y, SenGupta SK, Verma S, Members of the Breast Cancer Disease Site Group. Locoregional therapy of locally advanced breast cancer (LABC). Toronto (ON): Cancer Care Ontario (CCO); 2014 Sep 29. 124 p. (Program in Evidence-Based Care Evidence-Based Series; no. 1-19). [241 references]

### **Guideline Status**

This is the current release of the guideline.

The EVIDENCE-BASED SERIES report, initially the full original Guideline, over time will expand to contain new information emerging from their reviewing and updating activities.

Please visit the Cancer Care Ontario (CCO) Web site	for details on any new evidence that has emerged and implications
to the guidelines.	

This guideline meets NGC's 2013 (revised) inclusion criteria.

# Recommendations

## Major Recommendations

#### **Preamble**

Communication between oncologists, surgeons, radiologists, and pathologists is essential. A multidisciplinary case conference is the recommended forum for discussion of cases.

Any prior use of neoadjuvant therapy should be indicated when specimens are submitted for pathologic examination. Clinical details often affect the pathologic examination and interpretation, whereas details of pathology reports will determine appropriate treatment. Prior therapy (including neoadjuvant therapy) can change the nature of the specimen and what should be reported. The experience of the authors is that use of neoadjuvant treatment is frequently not indicated when submitting specimens.

It is recommended that surgical clips marking the original (pretreatment) turnour location be inserted before administration of neoadjuvant therapy. Neoadjuvant therapy may result in a change in the extent or distribution of turnour, including complete disappearance (clinically or pathologically complete response). The consensus reached at the Canadian Consortium for Locally Advanced Breast Cancer (COLAB) in 2011 was that clips should be inserted at the time of diagnosis to mark turnour location and that this should be considered the standard of care. Use of clips allows for

more accurate identification of the original tumour site (especially if there is complete response), resection of all (previously) cancerous tissue with adequate margins, pathologic interpretation of the most appropriate area of specimens, and greater accuracy of molecular analyses.

Question 1. In female patients with locally advanced breast cancer (LABC) with good response to neoadjuvant therapy, what is the role of breast-conserving surgery (BCS) compared with mastectomy?

#### Recommendation 1

For most patients with LABC, mastectomy should be considered to be the standard of care. (See Question 2b and 3 below for issues on axillary management and staging.)

BCS may be considered for some patients with non-inflammatory LABC on a case-by-case basis when the surgeon deems the disease can be fully resected and there is strong patient preference for breast preservation.

Question 2a. In female patients with locally advanced breast cancer who have had a mastectomy is radiotherapy indicated?

#### Recommendation 2a

Radiotherapy following mastectomy is recommended for patients with LABC.

Question 2b. In female patients with locally advanced breast cancer does locoregional irradiation result in higher survival and lower recurrence rates compared with breast/chest wall irradiation alone?

#### Recommendation 2b

It is recommended that patients with LABC receive locoregional radiation encompassing the breast/chest wall and local node-bearing areas following breast-conserving surgery or mastectomy.

Question 2c. In female patients with locally advanced breast cancer and pathologically complete response to neoadjuvant therapy is radiotherapy indicated?

#### Recommendation 2c

It is recommended that postoperative radiotherapy remains the standard of care for patients with LABC who have pathologically complete response to neoadjuvant therapy.

Question 3. In female patients with locally advanced breast cancer who receive neoadjuvant chemotherapy is sentinel lymph node biopsy (SLNB) or axillary dissection the most appropriate axillary staging procedure? Is SLNB indicated before neoadjuvant chemotherapy rather than at the time of surgery?

#### Recommendation 3-1

It is recommended that axillary dissection remain the standard of care for axillary staging in LABC, with the judicious use of SLNB in patients who are advised of the limitations of current data.

#### Recommendation 3-2

Although SLNB before or after neoadjuvant chemotherapy (NACT) is technically feasible, there is insufficient data to make any recommendation regarding the optimal timing of SLNB with respect to NACT. Limited data suggests higher sentinel lymph node identification (SLN ID) rates and lower false negative (FN) rates when SLNB is conducted before NACT; however, this must be balanced against the requirement for two operations if SLNB is not performed at the time of resection of the main tumour.

Question 4. How should female patients with locally advanced breast cancer who do not respond to initial neoadjuvant therapy be treated?

#### Recommendation 4-1

It is recommended that patients receiving neoadjuvant anthracycline-taxane-based therapy (or other sequential regimens) whose tumours do not respond to the initial agent(s) or where there is disease progression be expedited to the next agent(s) of the regimen.

#### Recommendation 4-2

For patients who, in the opinion of the treating physician, fail to respond or who progress on first-line NACT, there are several therapeutic options to consider including second-line chemotherapy, hormonal therapy (if appropriate), radiotherapy, or immediate surgery (if technically feasible).

Treatment should be individualized through discussion at a multidisciplinary case conference, considering tumour characteristics, patient factors and preferences, and risk of adverse effects.

# Clinical Algorithm(s)

None provided

# Scope

## Disease/Condition(s)

Locally advanced breast cancer (LABC)

Note: For purposes of this guideline, LABC includes Stages IIB and IIIABC and inflammatory cancer, as defined in the AJCC Cancer Staging Manual, 6th edition.

## Guideline Category

Evaluation

Management

Treatment

## Clinical Specialty

Oncology

Radiation Oncology

Surgery

## **Intended Users**

Physicians

# Guideline Objective(s)

To address several questions related to locally advanced breast cancer (LABC) and provide recommendations for treatment

## **Target Population**

Female patients with locally advanced breast cancer (LABC)

### Interventions and Practices Considered

- 1. Mastectomy
- 2. Breast-conserving surgery (BCS)
- 3. Radiotherapy
  - Following mastectomy or BCS
  - Following pathologically complete response to neoadjuvant therapy
  - Locoregional encompassing the breast/chest wall and local node-bearing areas

- 4. Axillary staging
  - Axillary dissection
  - Sentinel lymph node biopsy (SLNB)
- 5. Management of patients who do not respond to initial neoadjuvant therapy
  - Expediting to next agent of regimen
  - Second-line chemotherapy
  - Hormonal therapy (if appropriate)
  - Radiotherapy
  - Immediate surgery (if technically feasible)

## Major Outcomes Considered

- Disease-free survival
- Overall survival
- False negative results
- · Locoregional failure, relapse-free survival, and recurrence
- Lymphovascular invasion
- Pathologically complete response

# Methodology

### Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Hand-searches of Published Literature (Secondary Sources)

Searches of Electronic Databases

## Description of Methods Used to Collect/Select the Evidence

#### Literature Search Strategy

The literature was searched using the MEDLINE and EMBASE databases (1996 to December 2011) and the Cochrane Library. Several preliminary searches were conducted, before conducting the final overall search (see Appendix B in the original guideline document) which included and provided an update to all the preliminary searches (except two which were considered not relevant). In addition, the proceedings of the meetings of the American Society of Clinical Oncology (ASCO) and the San Antonio Breast Cancer Symposium (SABCS) were searched for relevant abstracts in the past three years. An Internet search of Canadian and international health organizations was also conducted to identify existing clinical practice guidelines, systematic reviews, and health technology assessments relevant to the guideline questions. The MEDLINE/EMBASE searches were rerun August 2013 and December 11, 2013 to locate articles published or indexed since the December 2011 search.

### Study Selection Criteria

The literature searches were designed to retrieve systematic reviews, meta-analyses, randomized control trials (RCTs), cohort studies, and clinical practice guidelines that studied locoregional therapy for locally advanced breast cancer (LABC). Studies had to include at least 50 patients (except for Question 4), have a prospective design, and provide a statistical comparison of the interventions of interest. Systematic reviews and meta-analyses had to include a description of the review methods (literature search, study selection, and data extraction). Only the most recent versions of reviews or guidelines were retained. Abstracts were discarded if a full-publication was also available, and only the most recent updates of RCTs were included, provided sufficient study details were reported.

For purposes of this guideline, LABC includes Stages IIB and IIIABC (including inflammatory cancer), as defined in the AJCC Cancer Staging

Manual, 6th edition. RCTs with Stage II (unspecified) were also included, as were studies with Stage IIA, as long as Stage I plus Stage IIA comprised less than half the patients, or there were subgroup results for Stage IIB and/or Stage III. Studies in which the title and abstract only indicated "early breast cancer" with no mention of stage or other indication that they may include patients meeting the authors' definition of LABC were excluded. An exception was made for RCTs located from another publication about LABC (review, guideline, or RCT); in this case the Methods and Results of the original RCT publication were reviewed to determine whether it did actually meet the authors' definition of LABC despite the title and/or abstract indicating otherwise. Studies in which the cancer was described as metastatic were excluded, unless mention was made that metastasis was only to regional lymph nodes. RCTs were the preferred studies. Cohort studies were considered in the initial screening, but were included only if the groups compared were equivalent (e.g., a similar distribution of tumour stage). Cohort studies were excluded if the patients were assigned to treatment based on patient/disease factors instead of randomly, such that prognosis of the two groups (before the treatment being studied) was not equivalent.

All studies identified through the literature search were assessed against the selection criteria by a health research methodologist (CW or GF) from the Working Group. Studies with uncertainty regarding eligibility were discussed with the other authors.

For Question 2b regarding extent of radiation (whole breast/chest or locoregional) studies were excluded if they focused on partial vs whole breast irradiation (e.g., accelerated partial breast irradiation [APBI], brachytherapy, intensity-modulated radiation therapy [IMRT]); intraoperative techniques such as TARGIT or ELIOT; compared radiation techniques such as dose-density, boost, or hypofractionation; or focused on simulation/treatment planning.

#### Results

The original searches in EMBASE and MEDLINE resulted in 6482 references, and the revised search (December 2011) found 23,629 additional references. The final updates (August and December 2013) found an additional 12,027 citations. Additional references (mostly results of older trials on postmastectomy radiation therapy [PMRT]) were located from the reference lists of included studies and recent reviews.

### Number of Source Documents

After applying the inclusion/exclusion criteria there were 143 publications of trials as well as 18 guidelines and 27 systematic reviews or metaanalysis that were relevant. Most studies included a mix of cancer stages. For example, for Question 2a, only two trials with PMRT were conducted exclusively with patients with Stage III breast cancer.

Methods Used to Assess the Quality and Strength of the Evidence

Expert Consensus

Rating Scheme for the Strength of the Evidence

Not applicable

Methods Used to Analyze the Evidence

Meta-Analysis

Review of Published Meta-Analyses

Systematic Review with Evidence Tables

# Description of the Methods Used to Analyze the Evidence

Quality Appraisal of Evidence-Based Guidelines

The SAGE Inventory of Cancer Guidelines is a searchable database of more than 2200 cancer control guidelines and standards released since 2003, developed and maintained by the Canadian Partnership Against Cancer's Capacity Enhancement Program (http://www.cancerguidelines.ca/Guidelines/inventory/index.php ). This inventory includes evaluation of the process of

practice guideline development and the quality of reporting using The Appraisal of Guidelines for Research and Evaluation II (AGREE II) Instrument.

#### Synthesizing the Evidence

When two or more trials provided appropriate data on outcomes of interest, statistical pooling using meta-analysis was done using Review Manager software (RevMan 5.1) provided by the Cochrane Collaboration. A random effects model was used for all pooling because it provides a more conservative estimate. Pooled results are expressed as relative risks (RRs) with 95% confidence intervals (CIs). A RR of less than one favours the drug/supplement and an RR of greater than one favours the placebo or control intervention.

#### Methods Used to Formulate the Recommendations

**Expert Consensus** 

## Description of Methods Used to Formulate the Recommendations

The Evidence-Based Series (EBS) guidelines developed by Cancer Care Ontario's Program in Evidence-Based Care (PEBC) use the methods of the Practice Guidelines Development Cycle. For this project, the core methodology used to develop the evidentiary base was the systematic review. Evidence was selected and reviewed by a Working Group of five members of the PEBC Breast Disease Site Group (DSG) and one methodologist. The systematic review and companion recommendations are intended to promote evidence-based practice in Ontario, Canada.

#### Formation of Guideline Development/Working Group

The Breast Cancer DSG asked the PEBC to develop a guideline on locoregional therapy in locally advanced breast cancer (LABC). In consultation with the DSG, a Working Group was identified from the DSG membership. This Working Group consisted of one surgeon, two medical oncologists, one radiation oncologist, one pathologist, and one health research methodologist. The Working Group and DSG also formed LABC guideline development group. This group would take responsibility for providing feedback on the guideline as it was being developed and acted as Expert Panel for the document at Internal Review, reviewing the document and requiring changes as necessary before approving it.

#### Research Questions

The Working Group developed the following research questions:

- 1. In female patients with locally advanced breast cancer with good response to neoadjuvant therapy, what is the role of breast-conserving surgery (BCS) compared with mastectomy?
- 2.
- a. In female patients with locally advanced breast cancer who have had a mastectomy is radiotherapy indicated?
- b. In female patients with locally advanced breast cancer does locoregional irradiation result in higher survival and lower recurrence rates compared with breast/chest wall irradiation alone?
- c. In female patients with locally advanced breast cancer and pathologically complete response to neoadjuvant therapy is radiotherapy indicated?
- 3. In female patients with locally advanced breast cancer who receive neoadjuvant chemotherapy is sentinel lymph node biopsy (SLNB) or axillary dissection the most appropriate axillary staging procedure? Is SLNB indicated before neoadjuvant chemotherapy rather than at the time of surgery?
- 4. How should female patients with locally advanced breast cancer who do not respond to initial neoadjuvant therapy be treated?

#### **Initial Recommendations**

Using the evidentiary base described in Section 2 of the original guideline document, the Working Group developed a set of initial recommendations. These initial recommendations were developed through a consideration of the aggregate evidence quality and the potential for bias in the evidence and the likely benefits and harms of BCS vs mastectomy, radiotherapy use or extent, and of SLNB vs axillary lymph node dissection (ALND). The Working Group considered the values they used in weighing benefits compared with harms, and then made a considered judgment. This process is described in detail for each topic area in the original guideline document.

## Rating Scheme for the Strength of the Recommendations

## Cost Analysis

A formal cost analysis was not performed and published cost analyses were not reviewed.

### Method of Guideline Validation

External Peer Review

Internal Peer Review

## Description of Method of Guideline Validation

#### Internal Review

Almost all Program in Evidence-Based Care (PEBC) documents undergo internal review. This review is conducted by the Expert Panel and the Report Approval Panel. The Working Group was responsible for incorporating the feedback and required changes of both of these panels, and both panels had to approve the document before it could be sent to External Review.

Expert Panel Review and Approval

The Breast Disease Site Group (DSG) acted as the Expert Panel for this document. The members of this group were required to submit conflict of interest declarations before reviewing the document. The document had to be approved by formal vote. To be approved, 75% of the DSG membership needed to vote or abstain; of those who voted, 75% had to approve the document. At the time of the voting, the DSG members could suggest changes to the document, and possibly make their approval conditional on those changes. In those cases, the Working Group was responsible for considering the changes, and if those changes could be made without substantially altering the recommendations, the altered draft would not need to be resubmitted for approval again.

The document was circulated by email to the DSG members on May 7, 2014 and all members responded by May 28, 2014. There were 18 votes and one abstention. Of the votes, there were eight approvals and nine additional approvals with some suggestions for consideration. One person did not approve unless changes were made. Approval was 94%; therefore, the guideline was considered to be approved by the DSG.

The Working Group considered all the feedback and made some changes to Section 1 in the original guideline document as a result. Almost all the comments were related to the definition of locally advanced breast cancer (LABC), and whether Stage IIB should be excluded or commented on separately. Although one reviewer preferred that Stage IIB be removed from the definition of LABC, the Working Group decided that it was not feasible or desirable to redo the evidence summary because most studies contained a heterogeneous patient group and extremely few dealt specifically with Stage III cancers. As suggested by one reviewer, we incorporated the footnote describing the rationale and limitations of the LABC definition into part of the text of Target Population (see page 1-2 in Section 1) because this is essential to the document and addresses some of the other comments. There was concern that Recommendation 1 stated modified radical mastectomy is the standard of care for LABC (i.e., for all patients with LABC), and that this did not really apply to patients with Stage IIB breast cancer. Although the Working Group did not feel it appropriate to list all situations in which breast-conserving surgery (BCS) may be considered, Recommendation 1 was modified to clarify that mastectomy does not apply to everyone, and the judgment of the surgeon (as well as patient preference) is required.

#### Report Approval Panel Review and Approval

The purpose of the Report Approval Panel (RAP) review is to ensure the methodological rigour and quality of PEBC documents. The RAP consists of nine clinicians with broad experience in clinical research and guideline development, and the Director of the PEBC. For each document, three RAP members review the document: the Director and two others. RAP members must not have had any involvement in the development of the guideline before Internal Review. All three RAP members must approve the document, although they may do so conditionally. If there is a conditional approval, the Working Group is responsible for ensuring the necessary changes are made; with the Assistant Director of Quality and Methods, PEBC, making a final determination that the RAP's concerns have been addressed.

In May-July 2014 the RAP reviewed this document. The RAP approved the document on July 29, 2014.

#### External Review

External Review by Ontario Clinicians and Other Experts

The PEBC external review process is two-pronged and includes a targeted peer review that is intended to obtain direct feedback on the draft report from a small number of specified content experts and a professional consultation that is intended to facilitate dissemination of the final guidance report to Ontario practitioners.

Following approval of the document at Internal Review, the draft document with recommendations modified as noted under Internal Review was circulated to external review participants for review and feedback.

#### Methods

Targeted Peer Review: During the guideline development process, ten targeted peer reviewers from across Canada considered to be clinical and/or methodological experts on the topic were identified by the Working Group. Several weeks before completion of the draft report, the nominees were contacted by email and asked to serve as reviewers. Seven reviewers agreed (two surgical oncologists, three radiation oncologists, two medical oncologists) and the draft report and a questionnaire were sent via email for their review. The questionnaire consisted of items evaluating the methods, results, and interpretive summary used to inform the draft recommendations and whether the draft recommendations should be approved as a guideline. Written comments were invited. The questionnaire and draft document were sent out on August 15, 2014. Follow-up reminders were sent at two and three weeks. The Working Group reviewed the results of the survey.

Professional Consultation: Feedback was obtained through a brief online survey of health care professionals who are the intended users of the guideline. Medical oncologists, surgical oncologists, surgeons (including general surgeons and plastic surgeons), radiation oncologists, pathologists, and advanced practice nurses in the PEBC database who had indicated breast cancer as an area of interest were contacted by email and directed to the survey website where they were provided with access to the survey, the guideline recommendations (Section 1) and the evidentiary base (Section 2). Participants were asked to rate the overall quality of the guideline (Section 1) and whether they would use and/or recommend it. Written comments were invited. The notification email was sent on August 19, 2014. The consultation period ended on September 16, 2014. The Working Group reviewed the results of the survey.

#### Results

Results of the Targeted Peer Review are given in Tables 10 and 11 in the original guideline document, while results of the Professional Consultation are reported in Tables 12 and 13 in the original guideline document. Concerns or suggestions for improvement along with the response of the authors are listed for both the targeted peer review and professional consultation. For professional consultation 28 responses were received: 10 medical oncologists, 4 pathologists, 6 radiation oncologists, 5 surgeons, and 3 surgical oncologists. Several indicated it is an excellent guideline.

# Evidence Supporting the Recommendations

## Type of Evidence Supporting the Recommendations

The recommendations are supported by randomized controlled trials, meta-analyses, clinical guidelines, and systematic reviews.

# Benefits/Harms of Implementing the Guideline Recommendations

### **Potential Benefits**

- Breast-conserving surgery (BCS) is considered to have generally better cosmetic effects and, for some female patients, may have less
  impact on body image, self-esteem, and sexuality than complete breast removal by mastectomy. With BCS there is usually no need for
  additional reconstructive surgery and the operation may be less complex.
- The Early Breast Cancer Trialists' Collaborative Group (EBCTCG) meta-analysis found that recurrence rates after radiotherapy were lower in patients with node-negative cancer compared to patients who did not receive radiotherapy. Recurrence rates with radiotherapy were also lower in patients with positive nodes both overall and in all subgroups analyzed. Radiotherapy improved survival rates in patients with positive nodes.

See the "Key Evidence for Benefits and Harms" section for each recommendation in the original guideline document for more information.

### **Potential Harms**

- In some cases of breast-conserving surgery (BCS) there may be positive margins requiring re-excision. The risks of recurrence and breast
  cancer mortality may be higher with BCS than mastectomy. There were no randomized control trials (RCTs) found to prove or disprove
  this. In cases of recurrence after BCS, further surgery may be needed and some patients would rather reduce this possibility by having
  mastectomy as initial treatment.
- Lymphedema is more likely when surgery includes axillary lymph node dissection (ALND) or/and when radiotherapy includes the nodal
  areas.
- ALND is more invasive surgery than sentinel lymph node biopsy (SLNB) and there is higher risk of surgical complications and of lymphedema occurring or being more severe. More than 80% of female patients undergoing ALND have at least one postoperative complication in the arm and psychological distress is common. In one study, ALND added to SLNB resulted in more wound infections, axillary seromas, paresthesias, and subjective reports of lymphedema than SLNB alone. Another study reported significant increase in upper and forearm circumference, higher subjective lymphedema, pain, numbness, and motion restriction for ALND compared with SLNB. Lymphedema is associated with cosmetic deformity, discomfort, infection, reduction in arm function, and emotional distress. Some people have allergies to the blue dye used in SLNB.

See the "Key Evidence for Benefits and Harms" section for each recommendation in the original guideline document for more information.

# **Qualifying Statements**

## **Qualifying Statements**

- Care has been taken in the preparation of the information contained in this report. Nonetheless, any person seeking to apply or consult the
  report is expected to use independent medical judgment in the context of individual clinical circumstances or seek out the supervision of a
  qualified clinician. Cancer Care Ontario makes no representation or guarantees of any kind whatsoever regarding the report content or use
  or application and disclaims any responsibility for its application or use in any way.
- See the original guideline document for qualifying statements related to each recommendation.

# Implementation of the Guideline

## Description of Implementation Strategy

An implementation strategy was not provided.

## Implementation Tools

Quick Reference Guides/Physician Guides

For information about availability, see the Availability of Companion Documents and Patient Resources fields below.

# Institute of Medicine (IOM) National Healthcare Quality Report Categories

## IOM Care Need

Getting Better

Living with Illness

### **IOM Domain**

Effectiveness

# Identifying Information and Availability

## Bibliographic Source(s)

Brackstone M, Fletcher GG, Dayes IS, Madarnas Y, SenGupta SK, Verma S, Members of the Breast Cancer Disease Site Group. Locoregional therapy of locally advanced breast cancer (LABC). Toronto (ON): Cancer Care Ontario (CCO); 2014 Sep 29. 124 p. (Program in Evidence-Based Care Evidence-Based Series; no. 1-19). [241 references]

## Adaptation

Not applicable: The guideline was not adapted from another source.

### Date Released

2014 Sep 29

# Guideline Developer(s)

Program in Evidence-based Care - State/Local Government Agency [Non-U.S.]

## Source(s) of Funding

The Program in Evidence-Based Care (PEBC) is a provincial initiative of Cancer Care Ontario supported by the Ontario Ministry of Health and Long-Term Care. All work produced by the PEBC is editorially independent from the Ontario Ministry of Health and Long-Term Care.

### Guideline Committee

Locoregional Therapy of Locally Advanced Breast Cancer (LABC) Working Group

## Composition of Group That Authored the Guideline

Authors: Muriel Brackstone, Glenn G. Fletcher, Ian S. Dayes, Yolanda Madarnas, Sandip K. SenGupta, Shailendra Verma, Members of the Cancer Care Ontario Breast Cancer Disease Site Group\*

\*See Appendix A in the original guideline document for a full list of members.

### Financial Disclosures/Conflicts of Interest

In accordance with the Program in Evidence-Based Care (PEBC) Conflict of Interest Policy, the guideline authors, Breast Disease Site Group (DSG) members, and internal and external reviewers were asked to disclose potential conflicts of interest. Of the Working Group, one author (MB) received a database grant from Roche Pharmaceuticals, is principle investigator of a trial on neoadjuvant chemotherapy and radiation, and published an opinion on surgical considerations in locally advanced breast cancer (LABC) patients receiving neoadjuvant chemotherapy; one author (ID) indicated the guideline could potentially increase the number of referrals for postmastectomy radiation therapy (PMRT).

For the Expert Panel, 14 members declared they had no conflicts of interest, and 5 declared potential conflicts. PB and DM declared grants or

other research support from pharmaceutical companies. DM also declared involvement as a principal investigator for clinical trials on a related topic. RG declared a travel grant from Roche to attend a conference. SD and MC declared managerial responsibility for a department that received funding from Roche for meetings. SD, MC, and DM published editorials/opinions on topics of this guideline.

The Report Approval Panel (RAP) declared no conflicts. Four targeted peer reviewers declared no conflicts. Of the others reviewers, JB received consulting fees from Roche, research grants/support from RNA Diagnostics, was principle investigator of related trials, and has co-authored a meeting report on neoadjuvant care in LABC; CS received research grants/support from Hoffman La Roche, was chair 2012-14 of the LABC Canadian National Consensus, and published commentary/opinions on LABC treatment and knowledge translation; and AA received a grant from Hoffman La Roche for LABC clinic, and published an opinion on surgical considerations in LABC patients receiving neoadjuvant chemotherapy.

The potential conflicts declared did not disqualify any individuals from performing their designated role in the development of this guideline, in accordance with the PEBC Conflict of Interest Policy. To obtain a copy of the policy, please contact the PEBC office by email at ccopgi@mcmaster.ca.

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This is the current release of the guideline.	
The EVIDENCE-BASED SERIES report, initially the full original Government and updating activities.	uideline, over time will expand to contain new information emerging from their
Please visit the Cancer Care Ontario (CCO) Web site to the guidelines.	for details on any new evidence that has emerged and implication
This guideline meets NGC's 2013 (revised) inclusion criteria.	
Guideline Availability	

## Availability of Companion Documents

Electronic copies: Available from the Cancer Care Ontario (CCO) Web site

The following are available:

Locoregional therapy of locally advanced breast cancer (LABC). Summary. Toronto (ON): Cancer Care Ontario; 2014 Sep 29. 18 p.			
Electronic copies: Available from the Cancer Care Ontario (CCO) Web site			
Program in Evidence-Based Care handbook. Toronto (ON): Cancer Care Ontario (CCO); 2012. 14 p. Electronic copies: Available fro			
the CCO Web site			

#### Patient Resources

None available

### **NGC Status**

This NGC summary was completed by ECRI Institute on June 18, 2015.

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